

**What is Claimed is:**

1. A method for treating a subject with a malignancy comprising the steps of:

- 5 sub A1  
108 p51
- (a) providing an expression construct comprising a promoter functional in eukaryotic cells and a polynucleotide encoding a *p53*, wherein said polynucleotide is positioned sense to and under the control of said promoter; and
- (b) contacting said expression construct with a tumor cell *in vivo*.

2. The method of claim 1, wherein said malignancy is a squamous cell carcinoma.

3. The method of claim 1, wherein the endogenous *p53* of said tumor cell is mutated.

15 sub A2  
15 type. 4. The method of claim 1, wherein the endogenous *p53* of said tumor cell is wild-type.

5. The method of claim 1, wherein said expression construct is a viral vector.

208 p52 6. The method of claim 5, wherein said viral vector is selected from the group consisting of a retroviral vector, an adenoviral vector and an adeno-associated viral vector.

7. The method of claim 6, wherein said viral <sup>expression construct</sup> vector is a replication-deficient adenoviral vector.

25 8. The method of claim 7, wherein said replication-deficient adenoviral vector is lacking at least a portion of the E1-region.

30 9. The method of claim 8, wherein said promoter is a CMV IE promoter.

10. The method of claim 1, wherein said subject is a human.

11. The method of claim 7, wherein step (b) is repeated at least once.

35 sub A3 12. The method of claim 11, wherein said tumor is resected following a repeated contacting, and an additional contacting is effected subsequent to the resection.

40 13. The method of claim 12, wherein said expression vector is contacted in a volume of about 3 ml, to about 10 ml.

Sub D2 14. The method of claim 11, wherein the amount of adenovirus administered in each contacting is between about  $10^7$  and  $10^{12}$  pfu.  
administration

sub A4 15. The method of claim 1, wherein said ~~contacting~~ is via intratumoral injection.

5 16. The method of claim 1, wherein said contacting is via injection into a natural or artificial body cavity.

17. The method of claim 16, wherein said injection comprises continuous perfusion of said natural or artificial body cavity.

10 18. The method of claim 16, wherein said ~~contacting~~ <sup>administration</sup> is via injection into an artificial body cavity resulting from tumor excision.

15 19. The method of claim 1, wherein the *p53*-encoding polynucleotide is tagged so that expression of *p53* from said expression vector can be detected.

20. The method of claim 19, wherein the tag is a continuous epitope.

20 21. A method for determining the effectiveness of a therapy on microscopic residual cancer comprising:

- 25 (a) providing a rodent with an incision into subcutaneous tissue;  
(b) seeding said incision with tumor cells;  
(c) treating said rodent with a therapeutic regimen; and  
(d) assessing the impact of said regimen on the development of tumors.

22. The method of claim 21, wherein said incision is sealed following step (b) and prior to step (c).

30 23. The method of claim 22, wherein said therapeutic regimen comprises introduction of a therapeutic composition into said incision, said incision being reopened after sealing and resealed after introduction of said therapeutic composition.

35 24. The method of claim 23, wherein said therapeutic composition comprises an expression construct comprising a promoter functional in eukaryotic cells and a polynucleotide encoding a *p53*, wherein said polynucleotide is positioned sense to and under the control of said promoter.

25. The method of claim 24, wherein said expression construct is a replication-deficient adenovirus and said promoter is a CMV IE promoter.

Add  
A5

add  
B9